Background: Comprehensive population-based data on ERCP utilization over the last 30 years in North America are lacking.

Objectives: To establish crude and age-adjusted population-based rates of ERCP, evaluate for changing indications for ERCP and evaluate for interactions between cholecystectomy technique and ERCP utilization from 1984-2009.

Design: Retrospective, comprehensive population-based study.

Setting: All inpatient and outpatient ERCPs and cholecystectomies in Manitoba, Canada from 1984-2009.

Patients: All residents of Manitoba, Canada with a history of ERCP and/or cholecystectomy.

Interventions: None

Main Outcomes: Yearly crude and age-adjusted rates of ERCP (diagnostic and therapeutic) and cholecystectomy (open, laparoscopic and with open bile duct exploration), and patient/procedure demographics.

Results: The rate of ERCP/10,000 people increased from 7.70 (1984) to 13.86/10,000 (2009) ($p = 0.001$). Diagnostic ERCP declined from 7.28/10,000 (1984) to 1.11/10,000 (2009), and therapeutic-ERCP (T-ERCP) increased from 0.42/10,000 (1984) to 12.75/10,000 (2009) ($p < 0.001$). ERCPs were more common in women (62%) and in older populations (60-79 years, >80years), with rates of T-ERCP reaching 62.58/10,000 in the elderly. The primary indication for ERCP has changed over time with biliary indications increasing from 50.3 to 67.3% and pancreatic indications decreasing from 18.3 to 8.1%($p<0.05$). The rate of T-ERCP increased during the transition from open to laparoscopic cholecystectomy (1991-1994) while open bile duct exploration (OBDE) decreased from 2.0 to 0.18/10,000 ($p<0.001$)

Limitations: Retrospective analysis, administrative data.

Conclusions: ERCP utilization has increased steadily from 1984-2009, and has changed from a diagnostic modality to a therapeutic one. Changes in cholecystectomy technique may have influenced T-ERCP utilization and likewise, the availability of T-ERCP has decreased the need for OBDE.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) was first developed in the early 1970's as a diagnostic modality for biliary and pancreatic disease[1]. The invention of endoscopic sphincterotomy (ES) in 1974 allowed ERCP to become a therapeutic modality as well[2, 3]. Over time ERCP has become increasingly performed for a variety of indications for both benign and malignant disease of the biliary tree and pancreas[4, 5]. Although the total number of ERCPs performed in the United States and Canada is unknown, it has been estimated that utilization has been increasing over time and that over 200,000 procedures are performed annually in the US alone[6]. Despite how common ERCP has become, little population-based data exist from North America documenting what type of patients (age, sex, rural vs. urban dwellers) are undergoing ERCP and for what indication.

Although, it is often stated that ERCP has evolved from a diagnostic procedure to a therapeutic one, there is a paucity of population based data to support this assumption aside from data showing that ERCP is becoming increasingly complex over time at tertiary referral centers[7] and inpatient ERCPs are more likely to be therapeutic in nature[8 9]. Also, if ERCP is now predominately a therapeutic modality, the reasons for this change have not been determined, although changes in cholecystectomy rate and technique and increasing rates of choledocholithiasis and pancreatic cancer have been postulated as causes[10, 11,12, 13]. Finally, recent US data suggest that rural patients may have a more difficult time accessing ERCP when compared to urban patients, but no population-based data exists to support this claim[12].

Given the lack of data available we set out to define changes in ERCP utilization, indication, and the population undergoing ERCP using a population based sample that includes academic, community and rural hospitals and providing doctors as well as comprehensive longitudinal health data for all patients. Additionally we set out to assess changes in the cholecystectomy rate and technique in the same population.

Methods

Manitoba Health (MH) is the single health insurance provider for every individual in the Province of Manitoba, Canada, and each individual has a unique personal health

identification number (PHIN) through which all health system contacts are recorded. MH is also the single payer for all physicians in Manitoba for all inpatient, outpatient and home physician visits. MH has been recording complete electronic administrative records since 1984, coding all outpatient physician-patient interactions using ICD-9 codes from 1984- 2009. MH also records all hospital claims for inpatient care using ICD9 (1984-2004), and ICD 10 (2004-2009) for diagnosis, procedures and surgeries. The data is de-identified by MH for research purposes to protect patient anonymity.

Institutional research ethics board approval was obtained prior to the initiation of this study. Additional approval from MH was obtained in order to ensure patient anonymity while safely accessing MH administrative databases.

These MH administrative databases have been used in other research to study inflammatory bowel disease, multiple sclerosis, colon cancer and diabetes in population based samples and have been proven to be highly accurate in several different validation cohorts[14-19]. Additionally MH regularly audits physician-billing claims for procedures to ensure the accuracy of all billings and adjust MD remuneration accordingly. Therefore there is a very low chance of errors in classification of procedures and surgeries within the MH databases.

Definitions:

Specific billing codes have existed for diagnostic ERCP (3505, 3506 (repeat ERCP)) since 1984 and an additional add-on code for therapeutic ERCP (3498) was introduced in 1987. Therapeutic ERCP (T-ERCP) is defined as any ERCP involving any combination of: endoscopic sphincterotomy (ES), biliary/pancreatic stent placement, endoscopic dilation (rigid or balloon dilation) of the biliary tree or pancreas or removal of pancreatic or biliary calculi.

The diagnosis at each ERCP was assigned by the providing MD at the time of each ERCP, and is required for remuneration. No standardized reporting system existed in the past in Manitoba. These post-procedure diagnoses are converted ICD-9/10 codes by MH.

Specific billing codes exist for cholecystectomy and cholecystectomy with open bile duct exploration (OBDE). ICD9/10 codes were used from the hospital admission data to differentiate open vs. laparoscopic Cx (LCx).

The province of Manitoba has a population of 1.25 million, that is comparable by way of baseline demographics (mean age, fertility rate, percent Caucasian race, and mean income) to the general population of the United States[20]. For the purposes of geographic assessment the province was divided into four regions (urban, north rural, south rural, mid rural) and each resident was assigned into one of these locations based on their residential postal codes. All ERCPs in Manitoba are performed in urban centers.

Subjects:

All persons in the province having undergone an outpatient or inpatient diagnostic or therapeutic (T-ERCP) between 1984-2009 were included in this study (ERCP cohort). All persons having undergone an outpatient or inpatient cholecystectomy (Cx) between 1984-2009 were also included (Cx cohort). The majority of procedures (97.3%) were present in both MD billing and hospital databases. Procedures were included in the analysis if they were present in both databases or in the hospital database alone, assuming that a small number of procedures may have been incorrectly submitted for billing by doctors (2.7% of procedures) and therefore not registered in the MH billing database.

Demographic information is available via MH registry file of which over 99% of residents belong.

Statistical analysis:

We evaluated longitudinal trends in ERCP utilization from 1984 to 2009. The results are presented and examined as the rates of ERCP and T-ERCP per 10,000 population. The crude rates of ERCP and T-ERCP were further analyzed by sex, age, and geographic region of residence (north rural, mid rural, south rural, and urban). The rates of ERCP were age and sex-standardized to the 2001 Canadian population to account for changes in the underlying make-up of the Manitoba population between 1984-2009. We compared the time trend by gender, age groups, and regional differences of ERCP and T-ERCP

performed in Manitoba by using logistic regression models, for the whole population and for males and females population separately, adjusting for age and region of residence. The odds ratio and 95% confidence intervals (CI) are reported here.

Results:

In total 31,607 ERCPs in 21,556 individuals have been performed between 1984-2009 and were included in the analysis. ERCPs were performed in the inpatient setting in 32.7% (n=8,634) of cases. The number of physicians providing ERCPs has fluctuated over time, with 3 in 1984, 6 in 1989, 11 in 1996, then decreasing to 7 from 2004 to 2009. ERCPS were performed in women 62.7% of the time (n=19,817), and the median age undergoing ERCP was 59 years (IQR 40-74) in women vs. 66 years (IQR 52-76) in men respectively with ERCP being more common in women than men across all of the years evaluated, OR 1.55(95%CI 1.51-1.60) ($p<0.0001$), Table 1. The rate of ERCPs/10,000 population has increased from 7.28 (1984), 11.28 (1994), 12.22 (2004), to 13.89/10,000 (2009), with a significant yearly increase in the rate of ERCP (OR 1.02 95%CI 1.01-1.03, $p<0.0001$) The crude rate of diagnostic ERCP has declined from 7.28/10,000 in 1984 to 1.11/10,000 in 2009 ($p<0.0001$), while the rate of T-ERCP has increased from 0.42/10,000 in 1987 to 12.79/10,000 in 2009 ($p < 0.001$), Figure 1A. Age standardized rates of diagnostic and therapeutic ERCP show similar changes with significantly increasing rates of T-ERCP in men and women and decreasing rates of diagnostic ERCP, Figure 1B.

Age and ERCP

ERCP utilization differed by age group over time between men and women, Figures 2A and 2B. In women, compared to those aged between 40 and 59 years, those aged 60-79 years (OR=2.06, 95%CI 1.98-2.15), and those aged over 80years (OR=3.17, 95% CI 3.01-3.34) were more likely to undergo ERCPs with peak rates of 38.79/10,000 and 62.68/10,000 respectively, Table 1. Rates in women increased significantly over time in age groups including (1-19, 20-39, 60-79 and 80+ years) but decreased slightly in the 40-59 year group ($p<0.01$ for all categories). In men, those aged 60-79 years (OR=3.37 95%CI=3.19-3.55), and those aged over 80 years (OR=6.90, 95%CI 6.45-7.38) were

more likely to undergo ERCPs and were also more likely to undergo any T-ERCP with peak rates of 35.13/10,000 and 88.05/10,000 population ($p<0.0001$). Different from women, rates of ERCP in men were unchanged over time in the 0-19 years, 20-39 years and 40-59 years ($p>0.05$ all groups) while the 60-79 and over 80 years groups increased significantly over time ($p<0.0001$ for both groups).

Geographic residence and ERCP

The time trend of age standardized ERCP utilization by geographic residence over time and separated by sex is shown in Figure 3A. Rates of ERCP in women and men were similar between urban, rural mid, and rural south from 1984-2009, which was continuously increasing (Table 2). After adjusting for gender, inhabitants of north rural (OR 1.84, 95%CI 1.75-1.94) and south rural (OR 1.07, 95% CI 1.03-1.10) were more likely than urban inhabitants to undergo ERCP. In comparison mid rural inhabitants were slightly less likely to undergo ERCP (OR 0.93 95%CI 0.90-0.97) when compared to the urban reference standard.

Indication for ERCP

ERCPs were performed most commonly for biliary indications (choledocholithiasis, cholangitis, bile leaks and biliary miscellaneous) at all time points between 1984 and 2009, increasing from 50.3% (1984) to 67.3% (2009, mean 58.7%) of all ERCPs ($p<0.01$), Figure 3B. ERCP performed to evaluate for acute and chronic pancreatitis decreased over time from 18.3% to 8.1% of cases ($p<0.001$) and undiagnosed abdominal pain decreased over time from 18.4% to 1.6% of all cases ($p<0.001$). ERCPs for malignant indications increased significantly over time from 1.4% to 5.1% of cases ($p<0.01$).

Cholecystectomy rate and technique

The yearly crude cholecystectomy rate was relatively unchanged over time dropping slightly from 20.08/10,000 (1984) to 19.46/10,000 (2009) ($p<0.01$), with a mean yearly rate of 20.70/10,000 population. As expected, the method of cholecystectomy was found to change dramatically from 0% of cases done as LCx (1984) to over 90% of cases being

done as LCx (1992-2009) in both women and men, Figure 4A. OBDE performed during Cx occurred at a low rate throughout the study period, with a peak rate in 1988 with 3.55/10,000 in women and 1.9/10,000 in men. A significant decrease in OBDE was seen after 1988, with rates then decreasing by greater than 95%, with a mean rate between 1999-2009 of 0.18 and 0.15/10,000 in women and men respectively ($p<0.0001$), Figure 4B.

Discussion

This study of ERCP utilization is the first population-based study in North America to describe ERCP utilization in a large and comprehensive population based sample, including both inpatient and outpatient ERCPs. We showed that ERCP use has steadily increased over time, having nearly doubled over the last 25 years, in spite of a considerable decrease in diagnostic ERCPs. We showed that the population undergoing ERCP is changing over time as well, with a significant trend towards elderly individuals undergoing ERCP, while the sex distribution has remained largely unchanged with a female predominance. We showed that the area of residence (rural vs. urban) did not have a clinically relevant impact on the rate of ERCP utilization, although statistically, northern and southern rural patients were at higher risk to require an ERCP. Finally we showed that although there has been a very slight decrease in the population rate of cholecystectomy, ERCP for biliary indications has increased over time. We postulate that this is related to an increased need for T-ERCP in the age of laparoscopic cholecystectomy, and this is underscored by the finding of a dramatic decrease in OBDE over time. The relative stability of the Cx rate over the duration of the study suggests that gallstone disease has not increased in the population, despite the rising incidence of obesity (a known risk factor for cholelithiasis).

The fact that we documented a significant and steady increase in the rate of ERCP over time is contrary to previously reported data from the US including the Manzen Jamal et al. Nationwide inpatient sample (NIS) study, which showed increasing rates of ERCP from 1988-1996 and then a significant decrease from 1997-2003[8]. They postulated that this decrease was related to increasing utilization of alternate, non-invasive diagnostic tests such as MRCP, endoscopic ultrasound and CT scanning. However, the NIS study was

limited to inpatient ERCPs, which may represent a more acute and/or chronically ill patient than the outpatient ERCP patient. In our study, less than one third of all ERCPs were done in the inpatient setting, which likely explains the differences in these results as we were able to capture all ERCPs, regardless of the location of the patient (inpatient or outpatient). In addition, although CT and MRI availability has increased over time in the province and EUS been available since 2004 (data not shown), the increase in ERCP utilization has still continued to increase on both a crude and an age standardized rate.

Our demonstration of relatively equal access to ERCP in both urban and rural areas in Manitoba is in contrast to recently published data from Shelton et al[12], showing significantly decreased ERCP access in rural areas in the US. The reasons for this apparent difference may relate to the structure and function of the single payer health care system in Canada. Specifically, rural areas in Manitoba are limited in scope of practice and very few endoscopy or surgical centers exist outside of urban centers, so patients are routinely sent to the tertiary referral hospitals for most surgeries and advanced procedures. In fact, the odds of having Cx or ERCP was higher in our Northern rural populations. We believe that this is secondary to increased cholelithiasis incidence in these areas due to the majority of residents in Northern Manitoba being of Native Canadian ancestry. Significantly higher rates of cholelithiasis has been shown in Native American populations throughout North America secondary to genetic differences in cholesterol metabolism and stone formation [21, 22]. Also as health resources are limited in much of the rural and northern areas of the province, individuals must come to urban centers for all aspects of advanced diagnostics (CT, endoscopic ultrasound, or MRI) or interventions, so referral bias for surgical or ERCP intervention should not be an issue. Finally, the fact that both Cx and ERCP were similarly elevated in these populations is reassuring that there is near universal access to ERCP despite the procedure being limited to mainly urban centers.

The increasing age of the population undergoing ERCP in our study is in keeping with other studies, showing increases in elderly and middle aged individuals undergoing ERCP more frequently than younger patients in recent years[8, 23, 24]. The reasons for this change are likely related to the overall aging of the population in Manitoba over this

time-frame, but may also reflect less aggressive surgical management of cholelithiasis in older populations, as decreased rates of Cx in the elderly have been observed in our population (data not shown). Additionally there are data to support a slow but steady increase in rates of pancreatic carcinoma and possibly choledocholithiasis over the last 20 years which in turn would contribute to increasing rates of ERCP utilization[12, 13].

This study has several limitations. Firstly an administrative database may inaccurately record diagnostic indications. Secondly, using ICD9/10 codes to assess the diagnosis at the time of the ERCP may well underestimate the rate of ERCP done for malignancy (i.e. jaundice as a diagnosis may often be malignancy related). Similarly, the lack of specific post procedure diagnoses used by many endoscopists may have led to an over representation of ICD 9 codes 575 and 576 (gallbladder and biliary tract miscellaneous), limiting our ability to comment on rates of ascending and sclerosing cholangitis, sphincter of Oddi dysfunction and bile leaks separately. This is further complicated by the fact that MH only stores the first 3 digits of ICD-9 codes for outpatient patient contacts, while storing all digits for hospital based contacts, making it impossible to accurately separate codes within the ICD9 code 576. Finally the fact that MH does not record current procedure terminology (CPT) codes to characterize inpatient and outpatient hospital interventions, limits our ability to elaborate more fully on the details of specific ERCP procedures (eg. we cannot tell if pancreatograms were performed or what type of therapies were performed in each case), and limits us to broadly describe ERCP as diagnostic or therapeutic in nature. However the endpoints we have used in this study would not be significantly altered by this information if it were available.

In conclusion, ERCP utilization has been steadily increasing over time from 1984-2009 and has evolved over time from a primarily diagnostic procedure to a therapeutic one. The reasons for this change have been driven by the change to laparoscopic cholecystectomy and in turn, increased ERCP utilization has decreased the need for open bile duct exploration during cholecystectomy. The rising rates are not likely secondary to increased rates of cholelithiasis since the CX rate has not appreciably changed. The population undergoing ERCP is more likely to be female, and overall the population

undergoing ERCP is aging. Access to ERCP in rural and urban areas appears to be comparable in this central Canadian province.

Take Home Message:

1. Contrary to prior published studies, ERCP use is increasing over time, and has changed from a diagnostic test to a therapeutic one.
2. ERCP rates are increasing for nearly all age groups in women (except for those 40-59 years) and are increasing among men older than 60 years only.
3. Changes in cholecystectomy technique may have resulted in increased ERCP utilization, and subsequently less use of OBDE.
4. The indications for ERCP have changed over time with increasing biliary indications and a marked decrease in ERCP for pancreatic indications and undiagnosed abdominal pain.

Acknowledgments

This study was funded by a grant from the Canadian Association of Gastroenterology and the Canadian Institutes of Health Research. Dr. Bernstein is supported in part by the Bingham Chair in Gastroenterology Research. The results and conclusions presented are those of the authors. No official endorsement by Manitoba Health is intended or should be inferred

Author Contributions:

Dana Moffatt: Study concept and design, analysis and interpretation of data, drafting manuscript, critical revision, obtained funding

B. Nancy Yu: Data acquisition, analysis and interpretation of data, critical revision, statistical analysis

Weichun Yie: Data acquisition, analysis and interpretation of data, critical revision, statistical analysis

Charles Bernstein: Study concept and design, analysis and interpretation, critical revision, obtained funding, study supervision

Grant Support: This study was funded by a grant from the Canadian Association of Gastroenteroloy and the Canadian Institutes of Health Research, received by Drs. Moffatt and Bernstein. Dr Bernstein is also supported in part by the Bingham Chair in Gastroenterology Research at the University of Manitoba, Canada.

Table 1: Patient demographics effect on Odds of undergoing ERCP, 1984-2009 (Male and Female combined)

	Number of ERCP (% of total ERCP)		Odd ratios	95% CI low	95% CI high	p
year	31,607		1.02	1.01	1.02	<.0001
Male	11,790	(37.30%)	reference			
Female	19,817	(62.70%)	1.55	1.51	1.60	<.0001
<=19	414	(1.31%)	0.06	0.05	0.06	<.0001
20-39	4,235	(13.40%)	0.61	0.58	0.63	<.0001
40-59	5,990	(18.95%)	reference			
60-79	8,099	(25.62%)	2.50	2.41	2.58	<.0001
80+	3,487	(11.03%)	4.11	3.94	4.28	<.0001
Inpatient ERCP	9,831	(31.10%)	reference			
Outpatient ERCP	21,776	(68.90%)	2.22	2.16	2.27	<.0001
Urban	19,202	(60.75%)	reference			
Mid rural	4,006	(12.67%)	0.93	0.90	0.97	<.001
North rural	2,188	(6.92%)	1.84	1.75	1.94	<.0001
South rural	6,134	(19.41%)	1.07	1.03	1.11	<.0001

Figure 1A and 1B: Crude and age standardized rates of diagnostic and therapeutic ERCP from 1984-2009

Figure 2A and B: Crude yearly rate of ERCP separated by age and sex

Figure 3A: Age standardized rate of ERCP by gender, 1984-2009

Figure 3B: Yearly percentage of common indications for ERCP 1984-2009

Figure 4A: Yearly rate of cholecystectomy by gender, and cholecystectomy technique

Figure 4B: Rate of open bile duct exploration compared to rate of therapeutic ERCP

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